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10. (Amended) An isolated nucleic acid of at least twenty bases hybridizable under high stringency conditions with a nucleic acid comprising a nucleotide sequence consisting of SEQ ID NO:3 (Figure 2). B

### REMARKS

Reconsideration of this application is respectfully requested.

In the Office Action, claims 1-8 and 10 were rejected under 35 U.S.C. §§§§ 101, 112, first and second paragraphs and 102(b). Claims 1-4 and 10 have been amended. The claims have been amended using language suggested by the Examiner in the Office Action. For example, claims 2, 3 and 10 have been amended adopting what the Examiner considered to be acceptable language for claiming nucleic acids and polypeptides. The amendment of claim 10, "high stringency" can be found in the specification on page 17, lines 21-24. Thus, no new matter has been added by this amendment. Claims 1-8 and 10 are pending in this application and are at issue.

In the Office Action, the Examiner stated that should claim 6 be found allowable, the Examiner would rejoin claim 9 with Group I claims (i.e., claims 1-8 and 10). Applicants respectfully submit that after entry of the present amendment, claim 6 (dependent from claim 4) is in a condition for allowance and claim 9 should be rejoined with claims 1-8 and 10 herein.

A courtesy copy of the claims pending in this application (after entry of the present amendment) is attached hereto as Exhibit 1.

The issues raised by the Examiner in the Office Action are summarized and

discussed below.

In the Office Action, claim 10 was rejected under 35 U.S.C. § 101 as the Examiner contended that because claim 10 recites "a nucleic acid" instead of "an isolated nucleic molecule" and because the claim does not recite an upper length limitation for the claimed nucleic acid, such a recitation encompasses a human chromosome in a human cell that has not been manipulated by the hand of man, thus a product of nature and not patentable under § 101. This rejection is respectfully traversed and reconsideration respectfully requested.

By the present amendment, claim 10 has been amended to call for "an isolated nucleic acid". As such, the claim no longer reads on a human chromosome in the human cell that has not been manipulated by the hand of man.

Therefore, Applicants respectfully submit that the rejection of claim 10 under 35 U.S.C. § 101 has been overcome and should be withdrawn.

Claims 2-3 and 10 were also rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim what Applicants regard as the invention. The Examiner contended that claims 2-3 and 10 were indefinite because it was unclear if the recitation of "as depicted in" is meant to encompass nucleic acid sequences comprising a sequence "within" SEQ ID NO:3, or which encodes a sequence "within" SEQ ID NO:4 or if full length sequence are intended. This rejection is respectfully traversed and reconsideration is respectfully requested.

Claims 2, 3 and 10 have been amended for the sake of clarity adopting the language suggested by the Examiner.

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application was filed, had possession of the claimed invention. The Examiner contended that the claims were not supported by an adequate written description since neither the claims nor the specification set forth what other structural features of an NRIF3 molecule are needed to exhibit the claimed function. The Examiner stated that the only structural limitation contained in claim 1 is the LXXIL sequence motif present in the C-terminal domain of the molecule and that the specification teaches that while the LXXIL motif is essential for the receptor specificity exhibited by SEQ ID NO:4, other (unidentified) regions of SEQ ID NO:4 are also needed for this specificity. The Examiner concluded that as shown by the results presented in the specification, the single structural limitation of the claimed invention, the LXXIL sequence motif in C-terminal end of the molecule, was not representative of the broad genus of nucleic acid molecules encompassed by the claims. The Examiner also stated that with regard to claim 10, the recitation that the claimed nucleic acid hybridizes to SEQ ID NO:3 under stringent conditions, encompassed not only a broad genus including genomic sequences, coding sequences, and allelic variants from any source, including mutants with an altered amino acid at every position of SEQ ID NO:3. This rejection is respectfully traversed and reconsideration is respectfully requested.

By the present amendment, claims 2 and 3 have been amended to be in independent form and claim the nucleic acid sequence and the amino acid sequence consisting of SEQ ID NO:3 (claim 2) and SEQ ID NO:4 (claim 3), respectively. Claim 1 has also been amended to depend from claim 3. Thus, the structural features of the regions required for the observed receptor specificity, full-length nucleic acids (and polypeptides encoded by the nucleic acids) are encompassed by the claims. The Examiner has

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Claim 10 was also rejected as being indefinite in the recitation of "stringent conditions" as the Examiner contended that this language encompasses different reaction conditions such that the degree of complementarity needed to achieve hybridization between the nucleic acid sequence claimed and SEQ ID NO:3 was unclear. This rejection is respectfully traversed and reconsideration respectfully request.

Claim 10 has also been amended to call for an isolated nucleic acid of at least 20 bases hybridizable under conditions of high stringency. Antecedent basis for this language can be found in the specification on page 17, lines 21-24 wherein the metes and bounds of the phrase are defined as follows:

"In a specific embodiment, "high stringency" refers to hybridization and/or washing conditions at 68°C in 0.2 XSSC, at 42°C in 50% formamide, 4 XSSC, or under conditions that afford levels of hybridization equivalent to those observed under either of these two conditions."

Claim 10 was also rejected as indefinite in its recitation of "a nucleic acid" instead of "an isolated nucleic molecule". As mentioned above in the section 101 rejection, this claim has been amended to call for "an isolated nucleic acid".

Therefore, Applicants respectfully submit that the rejection of claims 2, 3 and 10 under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

Claims 1-8 and 10 were also rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the

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admitted that these sequences are adequately described in the specification. On page 10 of the Office Action, the Examiner has stated (emphasis added):

"With the **exception** of SEQ ID NO:3 and 4, the skilled artisan cannot envision the detailed chemical structure . . ."

As for claim 10, by amending the claim to call for "high stringency" conditions, only exact matches in sequence are encompassed by this claim. The specification as filed teaches the use of such molecules at page 17, lines 16-18 as follows:

"A minimum length for a hybridizable nucleic acid is at least about 10 nucleotides, preferably at least about 15 nucleotides, and more preferably, at least about 20 nucleotides."

Regarding claim 10, Applicants respectfully submit that the specification clearly allows persons of ordinary skill in the art to envision the detailed chemical structure of the claimed nucleic acids. Such nucleic acids are greater than 20 nucleotides in length and can be used as probes and/or primers for the detection and quantification of NRIF3 sequences. Applicants respectfully submit that claim 10 calls for the nucleic acid itself without any functional limitations. For use as a probe or primer, its structure is any nucleic acid sequence of greater than 20 nucleotides which is contained in SEQ ID NO:3.

Applicants respectfully submit that amended claim 10 does not encompass mutants with an altered amino acid sequence at every position of SEQ ID NO:4. Such nucleic acids would not hybridize to SEQ ID NO:3 under conditions of high stringency (as defined herein) and as such are outside the scope of the claims. The skilled artisan can readily envision the detailed chemical structure of the encompassed polynucleotides

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regardless of the complexity or simplicity of the method of isolation.

Therefore, Applicants respectfully submit that the rejection of claims 1-8 and 10 under 35 U.S.C. § 112, first paragraph, has been overcome and should be withdrawn.

Claim 10 was also rejected under 35 U.S.C. § 102(b) as being anticipated by Leberer et al. The Examiner contended that since claim 10 recited a nucleic acid that need only have a minimum of 20 bases and need only hybridize to a nucleic acid having a sequence as "depicted in" SEQ ID NO:3 under non-specified stringent conditions, the claim reads Leberer et al. Leberer et al. was said to disclose a nucleic acid sequence wherein the complement of the nucleic acid sequence has 45.9% similarity to nucleotides 112-575 of SEQ ID NO:3. The Examiner concluded that since the claim did not recite any specific hybridization or wash conditions, and since the claim did not recite any functional limitations of the claimed nucleic acid that would distinguish it from the sequence taught by Leberer et al., the sequence taught by Leberer et al. anticipates the claimed invention. This rejection is respectfully traversed and reconsideration respectfully requested.

As mentioned above, amended claim 10 calls for hybridization under conditions of "high stringency". A nucleic acid having a 49% homology to the claimed nucleic acid would not hybridize thereto under these defined conditions.

Therefore, Applicants respectfully submit that the rejection of claim 10 under 35 U.S.C. § 102(b) is not well taken and should be withdrawn.

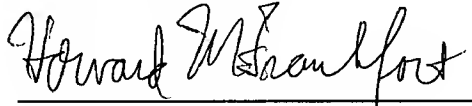
### **CONCLUSIONS**

Claims 1-8 and 10 are in a condition for allowance. Applicants respectfully request rejoinder of claim 9 with claims 1-8 and 10.

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In view of the above amendments and remarks, reconsideration of this application and issuance of a Notice of Allowance for claims 1-10 is earnestly solicited.

Respectfully submitted,



Howard M. Frankfort, Ph.D.

Reg. No. 32,613

Agent for Applicants

DARBY & DARBY, P.C.  
Post Office Box 5257  
New York, NY 10150-5257  
Phone (212) 527-7700

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Vandana YAJNIK; et al.

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For:

NRIF3, A NOVEL CO-ACTIVATOR FOR  
NUCLEAR HORMONE RECEPTORS

MARK-UP VERSION OF RESPONSE TO OFFICE ACTION

Hon. Commissioner of  
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Washington, DC 20231

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June 24, 2002

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Sir:

TECH CENTER 1600/2900

IN THE CLAIMS:

Please amend the claims pursuant to 37 C.F.R. § 1.121 as follows:

1. (Amended) [An] The isolated nucleic acid molecule of claim 3 further  
comprising a sequence that encodes a functional NRIF3 nuclear hormone receptor co-  
activator, wherein the NRIF3 binds in a ligand dependent manner to thyroid hormone

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receptor (TR) and retinoid X receptor (RXR), but does not interact with retinoic acid receptor (RAR), vitamin D receptor (VDR), progesterone receptor (PR), glucocorticoid receptor (GR), and estrogen receptor (ER) in a yeast two hybrid assay system or *in vitro*, or both, which polypeptide contains an LXXIL (SEQ ID NO:2) module in its C-terminal domain.

2. (Amended) An isolated nucleic acid comprising a [according to claim 1, wherein said NRIF3 has an amino acid] sequence that encodes an amino acid sequence consisting of [as depicted in] SEQ ID NO:4 (Figure 2).

3. (Amended) An isolated nucleic acid [according to claim 2, which has] sequence comprising a nucleotide sequence [as depicted in] consisting of SEQ ID NO:3 (Figure 2).

4. (Amended) A vector comprising the nucleic acid according to claim [1] 3, wherein said sequence is operatively associated with an expression control sequence.

10. (Amended) [A] An isolated nucleic acid of at least twenty bases hybridizable under [stringent] high stringency conditions with a nucleic acid [having a] comprising a nucleotide sequence [as depicted in] consisting of SEQ ID NO:3 (Figure 2).

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Pending Claims



1. The isolated nucleic acid molecule of claim 3 further comprising a sequence that encodes a functional NRIF3 nuclear hormone receptor co-activator, wherein the NRIF3 binds in a ligand dependent manner to thyroid hormone receptor (TR) and retinoid X receptor (RXR), but does not interact with retinoic acid receptor (RAR), vitamin D receptor (VDR), progesterone receptor (PR), glucocorticoid receptor (GR), and estrogen receptor (ER) in a yeast two hybrid assay system or *in vitro*, or both, which polypeptide contains an LxxIL (SEQ ID NO:2) module in its C-terminal domain.

2. An isolated nucleic acid comprising a sequence that encodes an amino acid sequence consisting of SEQ ID NO:4 (Figure 2).

3. An isolated nucleic acid sequence comprising a nucleotide sequence consisting of SEQ ID NO:3 (Figure 2).

4. A vector comprising the nucleic acid according to claim 3, wherein said sequence is operatively associated with an expression control sequence.

5. The vector according to claim 4 which is a plasmid.

6. A cell transfected with the vector according to claim 4.

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7. The cell according to claim 6 which is a eukaryotic cell.
8. The cell according to claim 7, which is a yeast cell.
9. A method for producing NRIF3 comprising culturing the cell according to claim 6 under conditions that permit expression of NRIF3.
10. An isolated nucleic acid of at least twenty bases hybridizable under high stringency conditions with a nucleic acid comprising a nucleotide sequence consisting of SEQ ID NO:3 (Figure 2).